INDIA.

Report from Bombay—Transactions of Service—Mortality from plague.

Acting Asst. Surg. Edward H. Hume reports, June 11, as follows:

	Week ended June 7, 1904.	Last week.
Plague attacks	91	118
Plague deaths	78	109
Plague mortality per 1,000	5.22	7.30
Smallpox deaths	12	16
Cholera deaths	0	0
Total deaths	524	578
Total mortality per 1,000	35.11	38.73

Plague deaths are less than 100 for the week for the first time since January 1.

A study of one hundred inoculations against plague.

By EDWARD H. HUME, M. D., *Acting Assistant Surgeon, U. S. Public Health and Marine-Hospital Service, Bombay, India.*

Object of the study.—This study was undertaken at the suggestion of Professor Haffkine, director, and of Dr. F. M. Gibson, superintendent, of the Government Plague Research Laboratory, Bombay, in order to determine:

1. The correct dose of Haffkine's prophylactic for children of various ages. Up to the present time the dose for children has been determined by taking an increasing fraction of the adult dose for each successive year until the full adult dose is reached at about the twenty-fifth year. In this way a child of five would receive one-fifth of the full adult dose, whatever that might have been determined to be for any given brew. It was felt that by this method a young child received a dose far smaller than it was capable of taking, and one, therefore, that did not give it the fullest possible protection.

2. The best hour at which to perform inoculation, (*a*) for the comfort of the patient, (*b*) in order to get the maximum reaction from a given dose.

3. Whether inoculation in children was dangerous in the presence of any preexisting disease, especially in children with a predisposition to tuberculosis.

Time and place.—The inoculations were all done on boys living in an orphanage conducted by the American (Congregational) Mission at Parel, Bombay. There had been a mild case of plague in the orphanage in October, 1903, and as there was a great deal of plague in the vicinity of the school the boys were about to be inoculated in any case. As they were all under one roof and under constant supervision, the observations were greatly facilitated. One hundred boys were inoculated in three groups, as follows:

Group I. Twenty at 10 a. m., on March 10, 1904.

Group II. Forty at 6 p. m., on March 26, 1904.

Group III. Forty at 2 p. m., on April 12, 1904.

Twelve days after the inoculation one of the teachers in the school was taken ill very suddenly with what was at first thought to be plague. He was at once removed to the plague hospital, but the symptoms subsided very rapidly and he was soon discharged as not having had plague. This teacher had been inoculated several years previously. None of the boys now treated had ever been inoculated before.

The prophylactic fluid.—The material used was supplied by the Plague Research Laboratory. This included not only the prophylactic fluid, but also the syringe and needles, a thermometer, and the necessary blanks for recording the observations.

Two separate brews of fluid were used, namely, brew No. 14659, to be spoken of in this study as brew A; and brew No. 13633, to be spoken of as brew B. The adult dose of each was given as 3 cc.

Previous health of the boys.—None of the boys were suffering from active pulmonary tuberculosis, although several of them had more or less bronchitis. As nearly all of the boys in the orphanage had been rescued during the severe famine of 1900, they were boys of weak constitution and had shown poor resistance to disease. Three had active cervical tuberculosis, one of them presenting a large bunch of swollen and tender glands in the left side of his neck. Only 22 of the 100 had a temperature below 99° F. at the time of inoculation, and none were to have been inoculated whose temperature registered 100° F. at that time, although it was afterwards discovered that 8 did reach that temperature. This was wholly due to bronchitis. Several of the boys had had smallpox, and others were still suffering from itch in rather a severe form.

Age groups.—The boys were divided into five age groups, and the number done in each group was as follows:

Age group 1. Three to five years	6
Age group 2. Six to seven years	14
Age group 3. Eight to nine years	32
Age group 4. Ten to eleven years	28
Age group 5. Twelve to seventeen years	20
	100

Method of inoculation.—The boys were given a thorough bath with soap and hot water just before the inoculation. They were then assembled in a room where the upper left arm of each was scrubbed with a 1 per cent solution of lysol before he went in to the inoculator, who worked in an adjoining small room. The syringe and needles were sterilized by boiling, and as each needle was used it was dropped into a pan of boiling water kept on a stove beside the inoculator. Thus no one was inoculated with a needle which had not been previously boiled just before using. The syringe was a large one, holding 20 ccm., so that with one filling it was possible to inoculate six or seven, according to the dose used. The needle was merely changed between each injection. The injection was given strictly subcutaneously, the skin being pinched up at the insertion of the left deltoid and the needle pointed toward the shoulder. As the needle was withdrawn a piece of cotton-wool was dipped in 1 per cent lysol solution and applied over the minute wound for fifteen minutes.

Observations.—Temperatures were taken every four hours, day and night, by several of the teachers who had been specially trained. At two of the periods the temperatures were taken by the writer. Two

thermometers were used—a Hicks half-minute (Kew certificate) and a Coxeter two-minute, both of London make. The two gave uniform results throughout. The boys were kept fairly quiet, staying most of the time on one of the wide verandas. They were allowed to sleep there as well, so as to be apart from the others. The diet was as usual, except in the case of those who had high fever, these being put, of course, on liquid diet for a time. The observations were continued for at least forty-eight hours, and a final record of the temperatures was made seventy-two hours after the start, when practically every boy had a normal temperature.

THE REACTIONS.

Constitutional reaction.

I. Fever. The limits of temperature were as follows:

Age group.	Not over 100 ° F.	Not over 100.5 ° F.	Not over 101 ° F.	Not over 101.5 ° F.	Not over 102 ° F.	Not over 102.5 ° F.	Not over 103 ° F.
	Cases.	*Cases.*	*Cases.*	*Cases.*	*Cases.*	*Cases.*	*Cases.*
1	5	....	1	.....	.....	.....	.....
2	5	3	6	.....	.....	.....	.....
3	4	2	15	3	2	2	4
4	3	4	3	5	5	7	1
5	3	1	2	7	2	2	3
Total	20	10	27	15	9	11	8
Brew A	.....	1	17	14	9	11	8
Brew B	20	9	10	1	.....	.....	.....
Total	20	10	27	15	9	11	8

Taking them in larger groups, in 57 the temperature did not exceed 101° F., while in 43 it was above 101, but not above 103.

As will be seen from the lower group of figures, brew B gave a lower set of temperatures than brew A, so that the age has nothing to do with the low records in age groups 1 and 2. This will be referred to more fully below.

The average temperature at the start was 99.15° F. This was not due to the fact that some of the inoculations were done at a late hour in the day, for the average temperature of those done at 10 a. m. was 99.23° F. (Unless otherwise stated, the averages given are those of 100 cases.)

Taking the 100 cases together, two waves of temperature were seen to occur during the period of observation. The first of these had its crest at a point fifteen to twenty hours after the start (16.4 hours in 100 cases), the second, forty to fifty hours after the start. The average highest temperature of the first wave was 101° F., and of the second, 100.13° F. The average highest point in the series was 101.07° F., reached nineteen hours after the start. Chart 2 shows that a certain number of the cases presented three waves of temperature. The four-hourly chart also shows that, observed continuously, the record placed the crests of the waves later and lower than when, as in chart 1, the crest of each separate case was taken and then compared with all the others.

The average of the lowest points was 98.67° F., reached thirty-seven hours from the start. In three cases the temperature did not go below 100° F. until seventy or more hours from the start. In chart 3 are

shown the widest variations from the average curve of 100 cases. Both the higher and the lower curves happen to have three waves. The higher is the record of a case inoculated with brew A, while the lower curve is that of one treated with brew B.

2. *General symptoms.*—Practically every case complained of headache and malaise soon after the start. These were in no case serious enough to need treatment, and if anything were less marked than they would have been in a similar series of adults.

Local reaction.—Suppuration did not occur in a single case. Every boy had a swollen and tender arm on the day after inoculation, although it was striking that there was less suffering than was commonly observed in adults. The axillary glands were enlarged in a number of the cases and one or two had a good deal of tenderness there.

The two brews of prophylactic.—Of the 40 cases done with brew B, there were some in each age group, while none of age groups 1 and 2 were done with brew A. Charts 1 and 2 bring it out very clearly that brew B gave decidedly lower reactions than brew A, even with the same doses. They also show that the weaker brew gave a more marked second wave, relatively to the first, than the stronger brew. The weaker brew also gave a more delayed reaction.

The dose of prophylactic.—Twenty cases were done as a preliminary series, boys of age group 3 being chosen, and a uniform dose of 2 ccm. given each one. As the average of the highest points was only 101.32° F., it was thought that a still higher dose could be given in this group, and accordingly, at the later inoculations, boys of this group received 2.5 ccm. This seemed to be a correct dose. The doses for the whole number were as follows (the adult dose for these brews being 3 ccm.):

Age group 1 (3 to 5 years), 1 ccm.
Age group 2 (6 to 7 years), 2 ccm.
Age group 3 (8 to 9 years), 2.5 ccm. (to 12); 2 ccm. (to 20).
Age group 4 (10 to 11 years), 2.5 ccm.
Age group 5 (12 to 17 years), 3 ccm. (to 6); 2.5 ccm. (to 14).

The higher dose apparently gave no more discomfort than the lower. The higher dose, therefore, may be regarded as the safe dose for each age group. This makes the dose for children much higher than by the old rule. For where by that a child of 3 years would have been given three twenty-fifths of the adult dose, or nine twenty-fifths of one cubic centimeter in a case where, as here, the adult dose was 3 ccm., in the present series he received 1 ccm. and showed no ill effects.

Charts 7 and 8 show that the reactions in age group 1 were lower than those in group 2, and thus indicate that the dose of 1 ccm. was probably too small for boys of 4 or 5, if boys of 6 could stand 2 ccm. so easily. These charts also show that just as the second wave is relatively stronger when a weak brew is used, so also a weaker dose than can be borne is followed by a relatively stronger second wave.

Age groups.—If the time of day at which inoculation was done, the brew of prophylactic, and the dose, be taken into consideration, the reaction in one age group differed very little from that in any other or from the average for the entire series. Thus in chart 6, although the reactions for groups 3 and 5 are slightly higher than the average reaction for the 100 cases, it is due to the fact that the average includes the reaction in 20 cases (age groups 1 and 2) done entirely with brew B.

Chart 5 shows that reactions obtained in several age groups with the same dose of the same brew varied little from each other.

In other words, if the dose were adjusted with reference to certain limits, young boys stood the inoculation as well as older, and vice versa.

Charts 8 and 9, showing the reactions of cases treated with brew B, were prepared because age groups 1 and 2 were treated only with brew B. The temperatures are considerably lower than those obtained with Brew A; but as seen in charts 6 and 7, the differences of temperature between age groups are due to unequal adjustment of doses. Thus chart 8 shows that age group 1 received too small a dose, the average of the highest points being 0.37 of a degree lower than in age group 2. Chart 9 shows this still more clearly, the temperature curve from the 4th to the 36th hour being steadily higher in age group 2. This fact could only be noted by taking temperatures every four hours or oftener, small variations and the characteristics of the temperature wave being unnoticeable in records taken only at ten, twenty, and thirty hours after the start.

Time of day.—A most interesting fact is brought out in chart 10. It is that the time of day at which inoculation is done has a decided influence, not only on the height of the curve, but on its general character. The natural tendency of the body to show a lower temperature in the early morning than in the afternoon is very apparent. Compare, for example, in chart 10, the curve —, —, — with the curve —— —— ——, the former being the average curve for inoculation done at 10 a. m. Here the natural tendency toward elevation of temperature accelerates the action of the prophylactic, and the temperature rises rapidly till 6 p. m., and goes slightly higher by 10 p. m., reaching the crest of the wave in 10.4 hours from the start. It drops sharply again by 2 a. m., and still farther by 6 a. m., not, however, reaching the 99.5 mark. The afternoon rise again manifests itself and the crest of the second wave is reached in 30.6 hours after the start. A third wave is evident, with its crest at the 52d hour.

The curve for inoculations done at 6 p. m. is totally different. The influence of the prophylactic causes a rise for 8 hours, but between 2 and 6 in the morning following inoculation there is a slight drop in accordance with the natural tendency. From then on there is a striking rise to the crest of the first wave, 20 hours after the start, i. e., at 2 p. m. The fall to nearly 99° F. by 6 a. m. on the following day is striking, and is followed by a second wave, less marked than the first, with its crest again at 2 p. m., or 44 hours from the start. In other words, after inoculation late in the day, i. e., at 6 p. m., the tendency for a low temperature at 6 a. m. is only just evident on the morning after inoculation, the effect of the prophylactic being really steadily on the increase at that time, namely, 12 hours after the start; and the rise of the first wave is scarcely interrupted by the slight fall. No third wave occurs.

Further, the inoculation late in the day is more comfortable for the patient, the temperature not rising high enough (not over 100.31° in 60 cases) to interfere with sleep on the fore-night. The period of greatest discomfort is from 2 to 6 the next afternoon, and by bedtime the temperature has started to fall. Sleep is likely to be interfered with because of the soreness of the arm, but only during the second night. The second wave is much less trying than the first, and a third is usually escaped.

The hours of highest and lowest temperature.—Chart 10 brings out

the dissimilarity between the curves of temperature following inoculation at different times of the day, but chart 11, by rearranging them, shows their general similarity. In this chart the curves are so arranged that the observations for 10, 2, and 6 o'clock, day and night, fall into the same column, hour for hour. The red line averages 100 readings for each of these periods, viz, for 10, 2, and 6 o'clock, day and night, and the 3 curves are seen to follow the average in their general direction, eliminating only the first rapidly rising wave in the curve of inoculations done at 10 in the morning. As indicated in the foregoing paragraph the natural tendency for a morning fall and an afternoon rise manifests itself. Thus the highest point reached is at 2 p. m. on the second day, while the lowest during the period of observation is at 6 a. m. on the third day. At 2 p. m. on the third day is the crest of the second wave (the third for inoculations done at 2 p. m.), while at 6 a. m. on the second day is the first depression after the first rise in all the curves. This arrangement of the curves only confirms what was said above regarding inoculations late in the day, this time being unquestionably the most comfortable for the patient.

General effect of the inoculations.—Although the charts are not continued beyond the fifty-sixth hour, still all the boys were carefully examined on the fourth day and scarcely a trace of fever was observed. They were also watched for signs of other trouble, but no one seemed to have suffered in the slightest as a result of the inoculations. The tuberculous glands were not made more tender, and at the present writing, two months after the last inoculation, no evidence of harmful effect has been noticed, although a sharp lookout for such has been maintained. It may be said, therefore, that inoculation has practically no effect in a harmful direction, even on children of weak constitutions. This was a very gratifying result, for the writer had been given to understand by some who had seen a good many inoculations that in a considerable number of cases harm, often permanent, was done to children by inoculation.

Although the number of cases treated was not sufficiently great to warrant any very general conclusions, still, the following points were brought out clearly enough to be emphasized:

1. Records taken only at the tenth, twentieth, and thirtieth hours do not give data enough as to the effects of inoculation, as regards the most favorable time of day for the operation, the desirable dose, or the general character of the temperature chart.

2. Two distinct waves of temperature usually follow inoculation, with their crests between 2 and 6 o'clock in the afternoon, at whatever time of day the inoculations may be done. The crest of the first wave thus comes between 10 and 20 hours after the start, while that of the second follows about 24 hours later. If inoculation be done early in the day, there are usually 3 waves.

3. The dose of the prophylactic for children should be relatively larger than that for adults. The following doses were found safe for children of various ages, considering 3 ccm. as the standard adult dose. In other brews the dose could be easily calculated from this (standard adult dose, 3 ccm.):

For children 3 to 5 years old, 1 ccm.
For children 6 to 7 years old, 1.5 ccm. to 2 ccm.
For children 8 to 9 years old, 2.5 ccm.
For children 10 to 11 years old, 2.5 ccm.
For children 12 years and over, 3 ccm. or the full adult dose.

4. Inoculation done late in the day—say between 5 and 6 o'clock—gave the best results, both in comfort to the patient and in maximum reaction from a given dose.

5. Inoculation done aseptically has no harmful effect on the patient's health, however young he be, provided he have no acute disease at the time of the operation.

Report from Calcutta—Transactions of service—Cholera and plague mortality.

Acting Assistant Surgeon Eakins reports, June 16, as follows:

During the week ended June 11, 1904, bill of health was issued to the steamship *Schonfels*, bound for Boston and New York with no passengers and a crew of 62. The effects of the Lascars were disinfected and fumigated; rat guards were kept on the wharf lines while the vessel lay at dock.

During the week there were 36 deaths from plague and 7 from cholera in Calcutta. In Bengal, for the week ended June 4, there were 235 cases; 199 deaths from plague.

ITALY.

Reports from Naples—Inspection of vessels.

Passed Assistant Surgeon Eager reports, June 27 and July 4, as follows: During the week ended June 25, 1904, the following ships were inspected at Naples and Palermo:

NAPLES.

Date.	Name of ship.	Destination.	Steerage passengers inspected and passed.	Pieces of large baggage inspected and passed.	Pieces of baggage disinfected.	Number of steerage passengers recommended for rejection.
June 22	Citta di Napoli	New York	488	75	850	25
23	P. de Satrustegui	do	199	25	350	13
25	Sicilian Prince	do	229	40	420	3
25	Algeria	do	216	50	450	7

Annual statistics of Italian emigration to the United States—Plague and sleeping sickness in the Transvaal.

Week ended July 2, 1904:

NAPLES.

Date.	Name of ship.	Destination.	Steerage passengers inspected and passed.	Pieces of large baggage inspected and passed.	Pieces of baggage disinfected.	Number of steerage passengers recommended for rejection.
June 26	Prinz Oskar	New York	553	91	875	19
29	Liguria	do	316	55	715	12
July 1	Prinzess Irene	do	269	65	420	10
2	Patria	do	215	27	370	10

PALERMO.

June 26	Sicilian Prince	New York	195	75	250	22
26	Algeria	do	148	50	175	9